

In the Claims

1 (currently amended). A method for sequencing a polynucleotide, comprising the steps of:

(i) reacting a target polynucleotide with a polymerase-enzyme, wherein said polymerase is immobilized on a solid support, and complementary nucleotides, under conditions sufficient for the polymerase reaction; and

(ii) ~~detecting an effect consequent on the incorporation of a specific nucleotide complementary to the target polynucleotide~~ the interaction between the polymerase, the target polynucleotide, and each specific nucleotide complementary to the target polynucleotide that is incorporated into a nascent polynucleotide being synthesized as a result of the polymerase reaction, to thereby determine the sequence of the target polynucleotide, the detection being carried out by measuring a change in or absorption of applied radiation that occurs during the interaction ~~incorporation.~~

2 (previously presented). The method according to claim 1, wherein steps (i) and (ii) are conducted with each of the complementary nucleotides in turn, until incorporation is detected, and then repeated.

3 (previously presented). The method according to claim 1, wherein step (i) is conducted with all the complementary nucleotides present.

4 (currently amended). The method according to claim 1, wherein the ~~complementary~~ nucleotides comprise a 3' blocking group which is removed after the polymerase reaction.

5 (currently amended). The method according to claim 4, wherein the blocking group ~~can be~~ is selectively removed by pulsed monochromatic light.

6 (currently amended). The method according to claim 4, wherein the nucleotides comprise a further blocking group at the terminal phosphate group of the triphosphate chain, and the further blocking group is removed prior to the removal of the 3' blocking group.

7 (currently amended). The method according to claim 6, wherein the further blocking group ~~can be~~ is selectively removed by pulsed monochromatic light under conditions different from those required to remove the 3' blocking group.

8 (previously presented). The method according to claim 7, wherein the further blocking group is removed by pulsing the monochromatic light for a duration different from that required to remove the 3' blocking group.

9 (currently amended). The method according to claim 1, wherein step (i) further comprises introducing a competitive inhibitor of the polymerase ~~enzyme~~.

10 (previously presented). The method according to claim 1, wherein the target polynucleotide of step (i) is bound to the polymerase enzyme by a  $\beta_2$  dimer complex.

11 (currently amended). The method according to claim 1, wherein the polymerase is ~~an~~ *E. coli* DNA polymerase III or T7 polymerase.

12 (previously presented). The method according to claim 1, wherein the polymerase is a Taq polymerase.

13 (currently amended). The method according to claim 1, wherein the polymerase is a reverse transcriptase.

14 (previously presented). The method according to claim 1, wherein step (ii) comprises detection of a change in resonance signal over time.

15 (previously presented). The method according to claim 1, wherein the radiation is electromagnetic.

16 (previously presented). The method according to claim 15, wherein the electromagnetic radiation is in the infra-red spectrum.

17 (previously presented). The method according to claim 1, wherein the incorporation of a nucleotide is detected using NMR.

18 (previously presented). The method according to claim 1, wherein the polynucleotide is DNA.

19 (new). The method according to claim 1, wherein measurement is carried out using evanescent wave spectroscopy.

20 (new). The method according to claim 1, wherein the nucleotides are not labeled.

21 (new). The method according to claim 1, wherein the effect detected results from a conformation or mass change of the polymerase that occurs upon incorporation of the nucleotide.